

CLAIMS

1. The use of an optimized human or humanized chimeric monoclonal antibody, characterized in that:

- 5 a) it is produced in a cell line selected for its properties of glycosylation of the Fc fragment of an antibody, or
- b) the glycan structure of the Fc $\gamma$  has been modified ex vivo, and/or
- 10 c) its primary sequence has been modified so as to increase its reactivity with respect to Fc receptors; said antibody having i) a rate of Fc $\gamma$ RIII (CD16)-dependant ADCC of greater than 50%, preferably greater than 100%, for an E/T (effector cell/target
- 15 cell) ratio of less than 5/1, preferably less than 2/1, compared with the same antibody produced in a CHO line; and ii) a rate of production of at least one cytokine by a Jurkat CD16 effector cell or by a CD16 receptor-expressing effector cell of the immune system of
- 20 greater than 50%, 100%, or preferably greater than 200%, compared with the same antibody produced in a CHO line;
- for preparing a medicinal product intended for the treatment of pathologies for which the number of
- 25 antigenic sites or the antigenic density is low, or the antigens are relatively inaccessible to antibodies, or else for which the number of activated or recruited effector cells is low.

- 30 2. The use as claimed in claim 1, characterized in that the number of antigenic sites is less than 250 000, preferably less than 100 000 or 50 000 per target cell.

- 35 3. The use as claimed in either of claims 1 and 2, characterized in that said cytokines released by the optimized antibodies are chosen from interleukins, interferons and tissue necrosis factors (TNFs).

4. The use as claimed in either of claims 1 and 2, characterized in that the optimized antibody induces the secretion of at least one cytokine chosen from IL-1, IL-2, IL-3, IL-4, IL-5, IL-6, IL-7, IL-8, IL-9, IL-10, etc., TNF $\alpha$ , TGF $\beta$ , IP10 and IFN $\gamma$ , by the effector cells of the immune system, in particular those expressing the CD16 receptor.

5. The use as claimed in either of claims 1 and 2, characterized in that the antibody induces the secretion of IL-2 by Jurkat CD16 cells or of IFN $\gamma$  and IL2 by the CD16 receptor-expressing effector cells of the immune system, for a low number of antigenic sites present at the surface of the target cells or for a low number of antigens accessible to antibodies or for a low number of effector cells.

6. The use as claimed in one of claims 1 to 5, characterized in that the effector cell is a leukocytic cell, in particular of the NK (natural killer) family, or a cell of the monocyte-macrophage group.

7. The use as claimed in one of claims 1 to 5, characterized in that the effector cell is a Jurkat cell transfected with an expression vector encoding the CD16 receptor.

8. The use as claimed in one of claims 1 to 5, characterized in that the optimized antibody is prepared after having been purified and/or modified ex vivo by modification of the glycan structure of the Fc fragment.

9. The use as claimed in one of claims 1 to 5, characterized in that the optimized antibody is produced by cells of rat myeloma lines, in particular YB2/0 and its derivatives.

10. The use as claimed in one of claims 1 to 10, characterized in that the optimized antibody has a general glycan structure of the biantennary type, with short chains, a low degree of sialylation, non-  
5 intercalated terminal attachment point mannoses and GlcNAcs, and a low degree of fucosylation.

11. The use as claimed in claim 10, characterized in that the optimized antibody has an intermediate GlcNac  
10 content that is non zero.

12. The use of an antibody as claimed in one of claims 1 to 11, for preparing a medicinal product intended for the treatment of a pathology chosen from  
15 hemolytic disease of the newborn, Sézary syndrome, chronic myeloid leukemias, cancers in which the antigenic targets are weakly expressed, in particular breast cancer, pathologies associated with the environment that target in particular individuals  
20 exposed to polychlorinated biphenyls, infectious diseases, in particular tuberculosis, chronic fatigue syndrome (CFS), and parasitic infections such as, for example, schistosomula.